CHAPTER 8

Oncology Drug Production in Sub-Saharan Africa: The Challenge and Opportunity, with Evidence from India

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Introduction

Cancer is expensive for all concerned, as Chapters 3–5 confirmed. One core reason for its unaffordability is the price of chemotherapy. Chemotherapy is lengthy, physically demanding with difficult side effects,

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and emotionally and financially draining. The oncology medicines required are expensive for cash-strapped individuals and health systems, and in Sub-Saharan African countries those medicines are almost all imported. This chapter argues that the current context provides a major opportunity for Sub-Saharan African countries to invest in local production of some key oncology medicines. The chapter traces the most important contextual factors facilitating local investment including the rising need for these drugs; the structure of their international production, marketing and pricing that is sustaining higher than necessary prices; and the current post-pandemic trends and policies that are encouraging new investment and growth in local health industries in Eastern and Southern Africa including those needed for cancer care, in order to strength local health security (Chapter 7).

This chapter establishes the unaffordability of these medicines and identifies the import gap and supply chain challenges. It then uses research on the Indian and international market structure for generic oncology medication to evidence over-pricing and lack of effective competition to drive prices down. The chapter then assesses the emergent business opportunity for local production in East Africa and associated challenges faced by potential investors, drawing on discussions with local manufacturers and distributors. Finally, the chapter argues that there is an opening for a combination of ambition and initiative from an interest coalition of local stakeholders including policy makers to generate investment in oncology production in Eastern and Southern Africa, to benefit both patients and industrial development.

Unaffordability of Oncology Drugs

Access to oncology medication remains problematic for cancer patients in both countries where patients were interviewed. In Tanzania, oncology treatment is free of charge to uninsured patients in the public sector, but

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the availability of these essential medicines has fluctuated in recent years, and some patients recounted past struggles to buy some of the medication privately. One farmer, with an annual household income equivalent to USD 400 had found his required chemotherapy drugs unavailable and had paid a sum roughly equal to his annual income to buy them privately. He had funded this by selling family farming land. Another Tanzanian patient recounted that she could not afford the recommended drugs for her kidney cancer, which she would have had to purchase for approximately USD 2000 (two-thirds of the household annual income); she was therefore prescribed other available cancer medication.

In Kenya, we found that access to chemotherapy relied on insurance funding or private payment. The cost of a cycle of oncology medication could be very challenging for Kenyan patients, even those with some insurance coverage. Here are some examples of out-of-pocket payments for chemotherapy at public hospital cancer centres in Kenya. A young man, 35 years, self-employed, with cancer of the jaw, had paid out of pocket KES 40,000 (USD 392) for his first chemotherapy sessions. This came on top of tests and surgery costing USD 1340 equivalent, all paid out of pocket, totalling in all 1.5 times the household's annual income. A prostate cancer patient, 51 years old and self-employed, in a very low-income household, had National Health Insurance Fund (NHIF) coverage but it was incomplete. He had topped up KES 78,000 to complete five chemotherapy cycles, a sum roughly twice the household's annual income. A 76-year-old breast cancer sufferer had paid 49,000 shillings (USD 480) for nine cycles of chemotherapy, equivalent to 13% of her household's annual income. A 58-year-old woman with breast cancer who did not wish to declare her household income stated that the NHIF had covered payments of KES 80,000 (USD 784) for eight sessions of chemotherapy, and commented, "the medication is very expensive when it is not available at the hospital [i.e. has to be purchased privately]". A retired professional woman, a breast cancer sufferer, recorded a total NHIF payment of KES 105,000 (USD 1030) for eight chemotherapy sessions.

A complete chemotherapy cycle will thus cost at least several hundred dollars if paid out of pocket or by a national health insurance fund, and the price may run into thousands. The financial demands may rise to multiples of household income, and they come on top of other payments for tests and surgery (Chapters 4 and 5). These are very large sums for low-income populations: in Kenya, the median consumption expenditure

per head in 2015/16, three years before our interviews, was 1.8 dollars a day (KNBS, 2018, p. 60); in Tanzania, the figure in 2017/18 was equivalent to USD 1 per day (MoFP- PED and NBS, 2019, p. 93).[1]

This unaffordability and financial toxicity for patients and families is replicated across Sub-Saharan Africa. In South Africa, it was recently calculated that the private price for a course of treatment for colorectal cancer was equivalent to 325 days of the minimum wage (Mattila et al., 2021). In 2018 the WHO calculated that a standard treatment for early-stage HER2-positive breast cancer would cost about 10 years of average annual wages in India and South Africa (WHO, 2018c).

The unaffordability of chemotherapy is also national, and not only concerns new patented treatments. Access to essential chemotherapy medicines remains poor across Sub-Saharan Africa. However, even standard, long off-patent oncology medications, if made available to all those in need, create a substantial burden on government and social insurance health funding systems (Gelband et al., 2016; Ngwa et al., 2022b). Rising cancer need will increase that burden on national health insurance systems, especially where, as in Kenya, many patients are persuaded to pay into insurance only once they become ill. While fully including cancer patients within financially fragile systems of universal health coverage will remain a huge challenge, there are nevertheless areas where costs could be reduced for national benefit. This chapter considers one such area: the scope for local production initiatives to produce essential oncology drugs to help reduce some of the identified costs and tackle some supply gaps, and the facilitative policy changes that would be required.

Import Reliance and Supply Chain Risk

Sub-Saharan Africa is almost completely reliant on imports for its access to essential oncology medication. The pandemic, as Chapter 2 has shown, focused minds on the supply chain risks inherent in extreme import dependency. The pandemic impact on cancer care in African contexts remains to be fully investigated but is likely to have been profound (Martei et al., 2021; Nnaji & Moodley, 2021). Even before the pandemic, however, the authorities in Tanzania and Kenya were well aware of supply chain gaps, and the risks and uncertainties of extreme import reliance for oncology medicine procurement. Kenyan interviewees noted that Kenya had developed an essential medicines list for cancer medication, alongside new treatment guidelines (Chapter 7). These exercises had identified

an initial list of 52 essential cancer products for an invitation to tender. However, that tendering exercise had resulted in purchases of only 38 of the required 52 items. None of these essential items were high-priced biologic medications. The procurement problems encountered by the Kenyan public sector buyers included a lack of registrations since some potential suppliers abroad had not registered the products in Kenya. However, the more challenging problem cited was that "the quantities were not lucrative": that is, the Kenyan orders were too small to interest external suppliers. Some of these items were later successfully sourced, but the supply constraints remain. We return to the implications for procurement policy below.

For East African cancer care, which oncology products are currently the most important for ensuring continuous high-quality supply at low cost? This question can feel invidious since all products are important to particular patients when that is what they need. However, some oncology products are "workhorses" with many applications. The WHO has developed, and regularly updates, a list of essential cancer medication (WHO, 2021b). For analysis of trade and pricing in this chapter, we have selected a subset of these, drawn from two East African expert sources (Table 8.1). In Table 8.1, the first column lists the "top ten" required medications identified by an experienced local oncologist. The second column list was developed by a local pharmaceutical manufacturer who had been investigating, with expert support, which oncology medicines were of particular local market importance in East Africa and had local production potential.

These medicines are all off-patent and are regarded by local and other clinical experts as key inputs to first line and continuing cancer treatment appropriate for lower income contexts. Furthermore, these medicines are predicted to continue in widespread use in the near future. We have added to this list one biological medicine, Trastuzumab, also off-patent, which is included, in originator and biosimilar formulations, in the WHO's priority list for the treatment of HER2+ breast cancer (WHO, 2021b). These medicines, widely produced in generic formulations, have as the final column shows a wide range of applications for highly prevalent cancers.

East Africa is 100% reliant on imports of these products. There is currently very little local production of oncology drugs in Sub-Saharan Africa as a whole. In South Africa, Fine Chemicals, an Aspen subsidiary, produces the API for Vincristine, a drug with a spectrum of uses in oncology.[2] Aspen also opened in 2018 a sterile facility for the production of cytotoxic medication in Port Elizabeth.[3] The initial production plans

Table 8.1 Some key oncology medicines for the East African market: main applications

Generic name: active ingredient	*Local oncologist's priority list (2019)*	*Local manufacturer's potential product list (2019)*	*Main application(s)*
Cyclophosphamide	X	X	Numerous
Methotrexate	X		Numerous
Fluoro Uracil (5FU)	X	X	Cervical, Breast, Colorectal
Doxorubicin	X	X	Numerous
Docetaxel	X	X	Numerous
Paclitaxel	X	X	Numerous
Gemcitabine	X	X	Numerous
Etoposide	X		Numerous
Cisplatin	X	X	Numerous
Goserelin		X	Breast, prostate
Bicalutamide		X	Prostate
Oxaliplatin		X	Colo-Rectal
Carboplatin		X	Ovarian
Tamoxifen		X	Breast
Anastrozole/Letrazole		X	Breast
Temozolamide		X	Brain
Vincristine		X	Numerous
Epirubicin		X	Numerous
Capecitabin		X	Numerous
Trastuzumab			Breast

Source Interviews

included Melphalan (under Aspen's brand name Alkeran), an anti-cancer agent with a number of applications. Aspen, a large South African-based multinational pharmaceutical company, has cancer APIs capability also in the Netherlands, allowing it to envisage an expanded and vertically integrated cancer portfolio.[4]

Otherwise, reliance by Sub-Saharan African governments on imported oncology medicines is complete. However, data on the current sources of imports of cancer medication into Eastern and Southern Africa remain poor. Available international trade data[5] do not provide a breakdown of international trade by cancer products: oncology medicines are included in a residual category,[6] after major medicine categories including antibiotics and anti-malarials are separately classified. The value of imports in this residual category in 2019 was large: USD 410 million for Kenya;

USD 219 million for Tanzania; USD 226 million for Uganda; and USD 1.4 billion for South Africa, but we cannot separately identify oncology drugs.

India as Oncology Supplier and Benchmark

India is an important supplier of essential oncology medicines to Eastern Africa. Indian exports, as a historically cheaper source of generic medicines, have dominated medicines imports into East Africa more generally (Chaudhuri et al., 2010; Mackintosh et al., 2018b). This dominance appears to be reflected in oncology medicine imports, benefitting from lower Indian prices,[7] even though data are incomplete. Detailed Indian export data can therefore provide some insight into the current import cost of essential cancer drugs for East Africa.

India is a major global exporter of anti-cancer medicines, with an export value of USD 757.34 million in 2019/20.[8] These exports reflect the pattern of cancer medicines access globally: 80% went to Europe and the Americas; just 6.1% (USD 46.1 million) went to the whole of Africa. The value of oncology imports from India into Kenya in 2019/20 (that is, largely before the Covid-19 emergency constrained the trade) was USD 1.67 million; into Tanzania USD 1.12 million; into Uganda USD 0.24 million; and into South Africa USD 10.07 million[9]: small shares of total medicines imports.

India's oncology drug exports to Africa were furthermore quite concentrated in a few countries: Table 8.2 evidences these concentrated export links for the medicines listed in Table 8.1, showing that India exports these medicines largely to East Africa, South Africa and some countries in North Africa.

Furthermore, these Indian export data confirm the market importance of some of the medicines listed in Table 8.1. In 2019/20 for example, 57% of Tanzania's oncology drug imports from India consisted of these categories: paclitaxel and docetaxel; actinomycin, dactinomycin and doxorubicin; and L-asparaginase, cisplatin and carboplatin. That share for Kenya was 24%, Uganda 29% and for South Africa just 23%. Furthermore, the values of these oncology imports from India, while showing erratic movement over time, have been growing between 2011/12 and 2020/21 at an annual rate of 16.5% in Kenya, 18.7% in South Africa and 2.4% in Tanzania.

Table 8.2 India's exports of oncology medicine to Africa, 2019/20, top country destinations for some key products

Product	*No of receiving countries*	*Top 5 recipient countries*	*Share of top 5 countries*
Cyclophosphamide	3	Ethiopia, Kenya, Tanzania	100
Methotrexate, 5-fluorouracil(5-fu) and ftorafur	10	Ethiopia, Sudan, South Africa, Kenya, Angola	89
Bincristine and vinblastine	7	Morocco, Ethiopia, South Africa, Botswana, Kenya	87
Paclitaxel and docetaxel	23	Morocco, South Africa, Tanzania, Egypt, Ethiopia	80
Etoposide	9	Ethiopia, Djibouti, Angola, Kenya, Mozambique	73
Actinomycin d (dactinomycin) and doxorubicin	16	South Africa, Tanzania, Nigeria, Egypt, Kenya	87
L-asparaginase, cisplatin and carboplatin	20	Algeria, Ethiopia, Egypt, South Africa, Tanzania	73
Tamoxifen	2	Angola, Mozambique	100
Other anti-cancer drugs	31	Algeria, South Africa, Morocco, Kenya, Ethiopia	88

Source Calculated from the DGCI&S database (from: https://tradedx.cmie.com/, June 2022)

We have no comparative data on oncology imports into East Africa and South Africa from other exporters including those from high-income countries. However, since India is generally a low-cost medicines exporter, it would be the key competitor for local oncology manufacturing. It is also a potential source of direct overseas investment in oncology manufacturing in East Africa. As such India provides a useful benchmark for local production debate. What can we learn from Indian experience about the scope for local manufacturing to help to address supply constraints in oncology? We argue below that Indian and other international evidence suggests substantial scope, within current international markets for oncology medicines, for competitive local production in African countries.

Competition Failures in Generic Oncology Markets

Most oncology drugs on the essential medicines lists in East Africa and at the WHO are chemical not biological products which are long off-patent, and their production is well understood. Furthermore, those products are widely produced globally, by generics companies in South Asia, Europe and elsewhere. The technology is widely available, and many of the required products can be produced and used in tablet form as well as intravenous products. The focus of this chapter on these widely produced generics contrasts with much of the international debate on access to cancer medication which has focused quite strongly, as reflected in several of our interviews, on legal constraints such as the TRIPS agreement to accessing innovator medicines under patent. While this latter concern reflects a serious issue for some categories of cancer patients, it should not displace a wider focus on continuing access constraints for cancer patients to the wide range of off-patent essential oncology medicines.

The international market for most essential oncology medicines is a market for branded generics: different manufacturers sell each medicine on private markets under their own brand name for that item. This international market is known to exhibit patchy competitive conditions and disorganisation. Prices have not been effectively driven down, as many expected, by the entry of many generic suppliers, and some key essential drugs still have only a few producers (WHO, 2018b). Furthermore, import prices paid for generic cancer medicines have historically varied very sharply by country, with lower income countries often paying above the best market price (Cuomo et al., 2017; WHO, 2018b). This evidence of market fragmentation suggests there is scope for collusive behaviour in the context of poor market information, poor regulation and disorganised public procurement processes.

These problems of high-priced generic oncology drugs are also experienced by high-income countries, which are starting to address the competition problems. In February 2021, after an investigation, the European Commission agreed a binding commitment by Aspen, the large South Africa-based generics multinational, to reduce the prices of six of its cancer medicines by an average of 73%.[10] All six had been off-patent for around 50 years. Sold under various brand names, they contain the active ingredients melphalan, mercaptopurine, chlorambucil, tioguanine and busulfan, with a wide range of uses. Aspen has also committed to

continue to supply these medicines, some of which are for small patient groups, having previously been accused of threatening to withdraw them from some European markets.[11] This investigation illustrates the continuing competition failures in the market for oncology generics, and also the potential role of both competition policy and effective procurement initiatives in addressing these market problems.

Competition Failures Within India

Market data for India confirm that, for the subset of drugs studied in this chapter, these competition failures occur also within the large and complex Indian medicines market. Within India, there are huge local disparities in the prices of key oncology medicines (Natarajan et al., 2020). The subset of oncology drugs studied in this chapter are all long-established in the Indian market. Table 8.3 demonstrates that many of these medicines have been available in the Indian private retail market for 20 or 30 years (Table 8.3 column 3). For almost all these medicines, there are many competing Indian and overseas firms selling into the Indian private market (Table 8.3 column 2). Note that the sales data (column 4) are for drugs sold by stockists primarily in the private retail market in India. The data do not include sales in the Indian institutional markets where drug products are purchased by procurement agents through a competitive bidding process (see further below).

None of these drugs in Table 8.3 are patent-protected in India, and seven were launched before the TRIPS agreement came into force. Only one drug—Trastuzumab—was introduced after India re-introduced product patent protection in pharmaceuticals in 2005, but this biological medicine is also not under patent in India. The importance of this subset of drugs is confirmed by Indian data since the listed drugs contributed about a third of the total Indian anti-cancer drugs retail market of Rs. 28,552.85 million (USD 408.3 million) in 2018–2019.

There is a large number of suppliers for almost all of these medicines in the Indian market (Table 8.3 Column 2). Competition is missing only for Goserelin: of two suppliers, AstraZeneca (European MNC) and an Indian firm (Bharat Serums & Vaccines), only AstraZeneca sold it in 2018/19. Only three other medicines have fewer than ten brands in the market (Table 8.3). Given this large number of sellers and the well-established technology for producing these drugs, the expectation might be these drugs should benefit from competitive pricing, with competition between

Table 8.3 Selected anti-cancer drugs: retail market sales in India, 2018–19

Drug	*No. of brands*	*Launch date in India*	*Retail sales 2018–19 (USD million)*[a]
Anastrozole	27	Apr-03	3.57
Bicalutamide	20	Jan-02	4.27
Capecitabine	30	Apr-04	6.50
Carboplatin	18	Feb-97	8.92
Cisplatin	22	Apr-90	1.50
Cyclophosphamide	14	Sep-00	1.82
Docetaxel	32	Mar-00	6.57
Doxorubicin	24	May-91	1.64
Epirubicin	23	Feb-98	1.82
Etoposide	11	May-91	0.28
Fluorouracil	7	Jul-81	0.16
Gemcitabine	28	Aug-00	6.37
Goserelin	1	Feb-97	2.95
Letrozole	64	Jul-01	11.42
Methotrexate	35	Dec-80	10.83
Oxaliplatin	27	Apr-00	5.53
Paclitaxel	45	Sep-98	19.99
Tamoxifen	17	Feb-86	1.01
Temozolomide	25	Jan-02	3.58
Trastuzumab	12	Jan-10	35.05
Vincristine	9	Feb-88	0.16
Total (these medicines)			133.93

Source Sales Audit Data, PharmaTrac of AIOCD Pharmasofttech AWACS Pvt Ltd (henceforth AIOCD-AWACS)

[a]INR/USD exchange rate 2018–19 average: Rs. 69.9229

sellers driving falling and convergent pricing. However, recent research in India has shown that oncology medication prices have not fallen, as a result of generic production and market competition, as far as would be expected from comparisons with other types of medication (Chaudhuri, 2019a, 2019b).

Detailed price data for the medicines in Table 8.3 confirm that these competitive effects on prices are not working in the Indian retail market. Prices for each of these medicines, for each particular formulation (e.g. a tablet of a certain strength), display vast variation. The median differential between the maximum and minimum retail price for the Table 8.3 medicines was 142%. These differentials varied hugely and were above

1500% for five medicines. The median differential between the retail price charged by the market-leading firm in each case and the minimum retail price was large at 117%, with five differentials over 500%. These differentials were not negatively correlated to the number of sellers; they are likely to reflect greater trust in some firms' brands than in others. An extreme case of price differentials in this sample of medicines is Anastrozole 1 mg tablet: the maximum price was Rs. 7718.75 (USD 108.87) compared to the minimum price of Rs. 27.20 (USD 0.38) (differential 28,277%). In this case, an innovator firm (AstraZeneca) has not been willing to reduce prices in India to match that of its generic competitors despite losing sales: the Indian market share of the product sold by AstraZeneca was only 3% in 2018–2019. These price differentials reflect competition failure, compounded by a failure of Indian government policies to reduce oncology market prices.

Effective Procurement as Competition Policy

What therefore can Indian experience teach about building more effective oncology markets and ensuring that competition does help to drive down prices? The key role of effective procurement in reducing prices and undercutting potential retail market collusion can be illustrated by the striking impact on prices achieved through effective public procurement in India.

A good example is provided by price data for the Tamil Nadu Medical Services Corporation (TNMSC). TNMSC is an agency of the Tamil Nadu state government for procuring and distributing medicines to different government organisations providing health services. It has earned a reputation as a successful and efficient medicine procurement agency. It procures medicines through a competitive bidding process, but the bids are restricted to those manufacturers who have the capacity and capability to supply quality medicines.

This is where the real market competition occurs. Table 8.4 shows the price impact. The table compares prices of selected like-for-like formulations between the private Indian retail market and the TNMSC achieved prices. The table shows that the price reductions achieved by the TNMSC are huge and consistent as compared to retail market prices. The median differential for this sample between the *minimum* retail price and the TNMSC price was 300%; between the market leader price and the TNMSC price the differential was 552%. In only two cases did the

TNMSC price exceed the minimum retail price despite strong quality standards.

These striking reductions show how competitive bidding for procurement orders, associated with the presence of several sellers, can make oncology medicines affordable. This evidence holds important lessons for East Africa. In the current situation of import dependence, fragmented procurement is further reducing the limited market leverage public buyers can exercise, helping to keep import prices high and reduce access. With few bidders for small procurement orders, a Kenyan interviewee with procurement experience noted the lack of leverage they experience:

> Few manufacturers for these commodities, it is the biggest challenge … it is like you need to do a lot of negotiation; if they were ten [suppliers bidding], you see you could even bring the price down.

Furthermore, in these circumstances of fragmented procurement, local importers in African countries may find scope to combine to keep prices high. In 2017, the South African Competition Commission opened an investigation of Aspen, Roche and Pfizer for suspected "excessive pricing" of six imported cancer drugs.[12] It was noted by the Commission that Aspen did not have any local competitors in this market, raising the scope for collaboration among importers. We return to local procurement strategies below. First, we consider whether the local manufacturers could find market space in a consolidating and growing East African oncology market.

The Scope for Local Oncology Manufacturing

The potential market in East Africa is growing as cancer cases rise. Prices are known to be a constraint on access to care (see above). Could local production of some of these medicines help to reduce prices in East Africa and increase the regularity of supply? There are reasons to think this might be possible, since the sheer lack of effective private competition, just documented for a key supplying country, is keeping generic cancer medicine prices high. This in turn suggests the existence of market space for local manufacturers to combine lower prices with sustainable profitability, once established.

Recent international initiatives to try to increase access to cancer medicines in Sub-Saharan Africa have not, to date, gone down this

Table 8.4 The price impact of good procurement in a fragmented oncology medicines market

Drug name	*Unit*	*TNMSC Price (USD)[b] (March 2019)*	*Retail Price of Market leader (USD) (Mid-2019)[b]*	*Price differential: retail market leader and TNMSC (%)[b]*	*Price differential: minimum retail and TNMSC (%)[b]*
Anastrozole	1 mg tablet	0.02	3.46	17,426	1843
Bicalutamide	50 mg tablet	0.06	0.69	1060	386
Capecitabine	500 mg tablet	0.20	1.87	817	−31
Carboplatin[a]	450 mg, 45 ml injection	5.15	35.51		
Cisplatin	10 mg injection 10 ml	0.62	1.02	64	46
Cyclophosphamide	200 mg injection	0.22	0.68	210	105
Cyclophosphamide	50 mg tablet	0.04	0.06	35	5
Docetaxel[a]	120 mg injection 3 ml	8.18	216.91		
Doxorubicin (Plain)	10 mg injection 5 ml	0.45	3.02	572	440
Epirubicin	10 mg injection	1.39	8.08	481	147
Etoposide	50 mg capsule	0.89	0.81	−10	-23
Fluorouracil	500 mg injection 10 ml	0.19	0.33	71	59
Gemcitabine	1000 mg injection	4.63	78.66	1600	624
Goserelin	3.6 mg injection	N/A	137.58		
Letrozole	2.5 mg tablet	0.02	0.55	2877	149

(continued)

Table 8.4 (continued)

Drug name	*Unit*	*TNMSC Price (USD)[b] (March 2019)*	*Retail Price of Market leader (USD) (Mid-2019)[b]*	*Price differential: retail market leader and TNMSC (%)[b]*	*Price differential: minimum retail and TNMSC (%)[b]*
Methotrexate	50 mg injection 2 ml	0.21	1.34	532	160
Methotrexate	10 mg tablet	0.10	0.17	68	60
Oxaliplatin[a]	50 mg injection 25 ml	5.19	66.84		
Paclitaxel	100 mg injection	3.17	70.52	2122	908
Paclitaxel	260 mg injection 43.4 ml	7.76	129.16	1565	679
Tamoxifen	10 mg tablet	0.01	0.04	219	86
Temozolomide	100 mg capsule	0.58	28.43	4781	566
Temozolomide	250 mg capsule	1.17	53.74	4512	326
Trastuzumab	440 mg injection	200.15	829.65	315	152
Vincristine	1 mg injection 1 ml	N/A	0.72		

Sources

1. For TNMSC prices, TNMSC website as follows. "Essential Drug 1 Year Rate Contract Details from March 2019" (https://tnmsc.tn.gov.in/user_pages/drugtender.php?drugcat=T18028) and "Essential Drug 1 Year Rate Contract Details from March 2019" (https://tnmsc.tn.gov.in/user_pages/drugtender.php?drugcat=T18028), accessed 11 November 2020
2. For Retail prices, AIOCD-AWACS database (see source Table 8.3)

Notes [a]For these products, the units are not exactly the same. For TNMSC prices, the units are: Carboplatin—10 mg, 45 ml injection; Docetaxel: 120 mg injection; Oxaliplatin: 2mg/ml
[b]INR/USD exchange rate 2019–20 average: Rs. 70.8970

route of supporting local production. As with previous global disease-focused initiatives, the focus has been on reducing the price of imported medicines, with philanthropic support. In 2017 the BMJ reported (Dyer, 2017, cited also in WHO, 2018b, p. 36) on an agreement negotiated by the American Cancer Society and the Clinton Health Access Initiative with Pfizer and Cipla to provide "at or near production cost price" to Ethiopia, Kenya, Nigeria, Rwanda, Uganda and Tanzania the following cancer drugs: docetaxel, doxorubicin, epirubicin, fluorouracil, gemcitabine, leucovorin, methotrexate, and paclitaxel (Pfizer); anastrozole, bleomycin, capecitabine, cytarabine, and vinblastine (Cipla); and carboplatin, cisplatin, and oxaliplatin (both). This was described as "a sustainable model of philanthropy" (Dyer, 2017). Cipla appears to have later dropped out of this initiative.

In 2021, an expanded "Cancer Access Initiative" was announced,[13] with four companies: Biocon Biologics (an Indian biotech), Novartis and Pfizer (innovator companies), and Viatris. The last is now the largest generics multinational, headquartered in the USA, formed by merging the generic arm of Pfizer with Mylan, a large US pharmaceutical company, which subsequently became a large API generic player by taking over an Indian firm, Matrix. The stated aim of the initiative is to generate savings of 60% on the purchase by low- and middle-income countries' governments of chemotherapy and hormonal medication for 30 cancers including a range of breast cancer regimens. The proposed reductions—very welcome in themselves—do indeed illustrate the scope for sustainable price cutting in generic oncology medication.[14]

These initiatives, which involve no technology transfer to African producers, also raise questions about sustainability, and the extent to which they could help to address health security concerns in crises including the recent pandemic and the next (Chapter 2). It is also an open question whether the initiatives, if effective, could undermine the market for local producers of oncology medicines, as has occurred through vertical programmes in the past (Mackintosh et al., 2018a). Some recent writers have characterised this issue as the need to avoid "onco-colonialism" when addressing access to cancer medicines (Hack et al., 2019).

The problem of high private market prices in India, noted above, appears furthermore, to be multiplied for those products when imported into East Africa. One interviewee in Kenya told a personal story. They

had recently taken a friend with cancer for treatment in India. On return, they spent KES 45,000 (around USD 400 at current exchange rates), for chemotherapy medication for three months' treatment. He commented:

> While that of course will cost him here around hundred and fifty thousand shillings [USD 1,325] to buy the same medicines. So it is cheaper to go, getting checked, buy medicine and come back.

This story aligns with other evidence of high import and procurement prices for oncology medication in Africa (Ngwa et al., 2022a; WHO, 2018b). If the cost of the imported medicine—by implication in this story, when prescribed in the private sector—was more than three times as high locally as when prescribed in India, then there is market space for local firms to both compete and lower prices.

Local Oncology Manufacturing: Market and Technical Challenges

In interviews with pharmaceutical producers in Tanzania, Kenya and also Uganda, respondents were asked whether they were planning to invest in the production of oncology medication. Just one manufacturer in Kenya stated that they had future plans to produce one anti-cancer medicine. All others said no. All firms saw oncology production as risky, both in practical and financial terms.

One manufacturer emphasised the physical risks:

> Cancer products are cytotoxic, so cancer products are actually killing your cells. … Because they are cytotoxic compounds, the whole aspect of handling the compounds, preventing cross-contamination, becomes a major critical issue and that's why no regulatory authority will allow you to make cancer products in the same facility where you're making, let's say, paracetamol. So if anybody is serious about manufacturing cancer products, they will have to think of putting up a new facility.

Another experienced manufacturer agreed about the risks involved:

> Cancer is not something that you are going to rush and start taking chances. It's a matter of life and death.

Many manufacturers' concerns focused on technical challenges and the implied scale of new investment. Oncology medication, they noted, required specialist plant and equipment to ensure sterile production of (mainly) intravenous medication. This in turn required very substantial investment, including modularity and partial automation to help keep staff safe, given the toxicity of the products. Greatly enhanced training and quality assurance—major changes in the culture of production processes—were required to achieve this upgrading, including major improvement of waste management capabilities:

> For cytotoxins … [you have] to make sure that they are decontaminated and that the waste is then stored and destroyed in a very specific manner.

One manufacturer in Kenya listed the key challenges for his firm for such a move: identification of the products (tablets, injectables); technology and machinery and the required production environment; methods, technical know-how and sources of inputs. This was a firm that had previously produced injectables but had then stopped; the interviewee also had experience of sterile production elsewhere. He reflected on his experience:

> Sterility is the issue and the requirements for sterile. … I know the challenges that are there. The kind of capital outlay you need to maintain the sterile environment is really huge and it requires a lot of discipline for you to be able to maintain the standard. So, the environment and the personnel are the main issue … the regulators … understand the seriousness … I would not allow anybody to set up the sterile plant unless they are sure they will maintain the standards.

Another manufacturer in Kenya noted that the infrastructure cost drivers, especially power, were particularly problematic for intravenous (IV) products:

> The main cost comes from two things, the power and the plastic. … plastic uses a lot of power. … if you are paying five times more on power how will you be competitive?

A manufacturer in Tanzania stated that oncology medicines production was possible with an international partner but still constrained by limited local production capabilities. These technical challenges all raised the need for technology transfer and learning from abroad. Table 8.5 lists systematically the challenges identified.

Table 8.5 Challenges for local manufacturing of oncology products

Challenge category	*Detail*
Technological	• Specialist equipment to manage toxic materials • Special plant configuration and contained use • Sources of API • Modularity as a key step in investing in oncology production • Automation as a key risk management approach to minimising contact with toxic raw materials • Cost of automation—and link to return on investment as key trigger for investors
Strategic	• Product portfolio choice and drivers, based on market intelligence • Information on acceptable cost of goods (COGS) and profitability parameters
Environmental Management	• Managing toxicity of production facilities • Waste management
Skills upgrading	• Management and documentation of sterile production • Staff training in handling sterile toxic products • Quality control and assurance • Laboratory skills
Markets or market signalling for investment	• Market intelligence • Market organisation, innovative procurement • Pre-orders, procurement contracts
Platform technologies	• Leveraging certain industry platforms, e.g. biosimilars (see Chapter 10)

(continued)

Table 8.5 (continued)

Challenge category	*Detail*
Government industry and trade policy	• Support for accreditation and export success • Commitment to local purchasing in practice • Trade policy that does not disadvantage local manufacturing against importing • Inter-government collaboration to guarantee regional procurement, to ensure sufficient market size for a local facility • Active problem-solving support for new investment and upgrading
Finance	• Affordable long-term finance for CAPEX (capital expenditure) for building new cGMP-compliant plants or upgrading existing plant • Affordable short-term finance for OPEX (operating expenditure) for day-to-day operations • Early-stage finance (grants, etc.) for technology incubation and maturation • Incentives for local manufacture and export (tax credit schemes, export guarantees, export pay-outs)

Source Authors

This is a formidable list. However, the challenges are not unfamiliar, and in most cases, the technical and managerial capabilities to address these challenges already exist in East African manufacturing. Technology transfer will require overseas partner firms, using a variety of potential institutional forms including new investors, joint ventures or licensing relationships. Long-term patient capital and government facilitation of the technology transfer are essential.

The list also includes challenges of market organisation and integration also addressed in Chapter 7. A new facility for intravenous oncology medication might cost, it was estimated by one interviewee, USD 20–25 million. Hence, the scale of demand, and the need to consolidate demand and overcome market fragmentation, were seen as key to estimating profitability and return on investment. Manufacturers told us that they lacked

knowledge of the choice of portfolio of products to produce, notably because both quantification of current use, and knowledge of treatment guidelines, were still limited among industrialists. This brings us back to the key role of procurement. More broadly, the formidable list of risks and challenges suggests a need for a major initiative from African governments to change the local market and—as it turns out—the international policy "weather" for local oncology manufacturing.

The Role of the Health System in Building Local Oncology Supply Chains

If health system policymakers and clinicians in East Africa are looking for scope to build more robust oncology medicines supply chains, including potentially local producers, then the health system needs to be an active player in building the local oncology market and industrial options. There are two strands to the initiative required: one international, one local.

The international aspect is clearly illustrated by the experience of one local manufacturer. Interested in investigating the scope for local oncology production, pre-Covid-19, he recounted a discussion with WHO health experts in which he was strongly counselled against the initiative. Their argument went, he recalled, that African countries should first learn to manage these drugs well within their health systems before moving on to local manufacture. A list of the required improvements in health system oncology capability included handling of drugs, staff safety in using toxic chemicals, avoiding cross-contamination during treatment, and managing waste.

In this, the WHO experts were reflecting a wider international viewpoint. For example, speaking in 2016, Pascal Soriot, head of AstraZeneca, is recorded as arguing that "there is no point giving free cancer drugs to Africa…[because]…it is not only a question of medicine, it is a question of infrastructure" (Lancet Oncology Editorial, 2017).

These are undoubted challenges in local cancer services, of which East African health professionals are keenly aware. An interviewee in one Kenyan cancer centre noted that many nurses were afraid of mixing and handling oncology drugs, being aware of their toxicity, and finding the protective clothing alarming, commenting: "There is a lot of stigma, when it comes to the preparation and administration of chemotherapy". That oncology clinic had initially improvised a filtration and extraction system with a chimney and ventilation. Recently they had received a

donated biosafety cabinet for mixing medication but had found that the filters needed very frequent changing because the lack of air conditioning required open windows, hence dusty air. They have requested an air conditioner but, the interviewee reflected:

> Things happen very slowly at the County level, so we are still waiting. So at the moment we still use the filter and the extractor, and I think if we still had the biosafety cabinet [i.e. it was functioning] we would still need to utilize the chimney because we are getting more and more patients for chemo, so we need to mix more and more chemos and the biosafety cabinet is such that one person can mix.

This discussion shows a clear local awareness of the need for secure handling, and the pressures that can undermine safety as patient numbers increase. It also reflects the importance of attention to the full range of requirements—including spare parts and working environment—needed to support equipment donation.

The interviews with health professionals attest to commitment to improving care at the facility level, and there are a number of initiatives underway in both Tanzania and Kenya to improve oncology management. The health facilities are treating rising numbers of cancer patients and expanding their capabilities, despite pandemic constraints. The number and range of cancer treatment centres are rising, and continuing weaknesses in the health system are being addressed, in some cases through external clinical partnerships. More generally, there has been push-back from African clinicians in recent years against these negative international views of local health system capability, emphasising local knowledge, training and skills to administer chemotherapy, and citing the active accreditation of facilities treating patients with chemotherapy drugs through inspection by health ministry regulators, using checklists to inspect handling and management of cytotoxic drugs.[15] Current international literature reflects more positive and supportive international attention to improving cancer care in Africa (Ngwa et al., 2022a) while health system challenges are not regarded internationally as an impediment to expanding access to medication.

Furthermore, challenges of oncology drug management at the health facility level constitute a curious argument to deploy against local manufacture of these medicines. Indeed, this argument could be turned on its head. A manufacturing firm establishing oncology drugs production

would have a strong incentive to work with oncologists, oncology nurses and other health experts to ensure that shared challenges such as keeping staff safe, avoiding cross-contamination, and managing waste disposal were applied right along the supply chain from producer to patient, since this would affect their accreditation and regulatory status. Such a firm would develop the technological and linkage capabilities to assist and support users in upgrading their knowledge and proficiencies while simultaneously learning from their users.

While the health system challenges are undoubtedly considerable, so are the potential benefits of local production. Manufacturers are aware that their employment and their own procurement of inputs feed back into and support the wider economy (Chapter 7). There are common skills to be developed along the entire supply chain in handling and using these medicines. Technology transfer can support manufacture, logistics handling, quality assurance and appropriate use right along the chain. Building the capability of one segment of the supply chain can feed back into and strengthen capabilities in another segment.

As the Indian evidence suggests, however, interventions are needed to consolidate demand and procurement and ensure procurement is used to manage the market. These interventions require collaboration between government and health system stakeholders, both public and private. In Tanzania, the National Health Insurance Fund covers cancer treatment and actively negotiates medicines prices with local pharmacies, achieving price reductions of around 25%.[16] Collaboration such as the Kenyan forum to create the essential medicines list and treatment guidelines that brought together public and private sectors can be further built on to develop market intelligence for investors. Procurement commitments, to buy for a number of years ahead, and consolidated procurement for regional markets require government initiative. Indeed cytotoxic cancer products are perfect candidates for public pool procurement initiatives, along the lines of the Tanzanian Medical Stores Department's lead role in the SADC pooled procurement initiative (Chapter 7). Health policy makers could also collaborate with manufacturers to refine a working list of the most appropriate medications for manufacturers' consideration: one interviewee, for example, suggested a small set of medicines widely used for the most prevalent conditions such as breast and cervical cancer. Oncology medicines production is a good example of the scope and imperative, discussed in Chapter 7, to raise industrial ambitions, including

identifying local firms' potential markets as regional and international within and outside Africa.

Conclusion

In the context of continuing and rapidly increasing need and demand for cancer medicines, the emergence of local manufacturers could help improve access, price and supply chain stability. The lessons from India identify scope for competitive production and pricing within currently high-priced and fragmented international markets. Indian experience also illustrates the scale of pricing benefits to be gained from organised larger scale procurement, even in relation to market prices in the Indian market. Scaling up procurement, however, requires collaboration between public, non-profit and private sector users, and between national governments, in order to increase orders and exert more market leverage on prices. The pricing benefits will then be felt region-wide. Philanthropic supply offers, welcome in the short term, should be carefully scrutinised for medium-term impact and against the building up over time of local manufacturing capability.

Regulatory regimes can be scrutinised for impediments to rapid registration of imports where desirable, and clarity on technical requirements. Production of generic oncology medication can build effectively on the existing technological capabilities of local firms, creating skills that can also feed into health system capabilities. Major new plant investments are required for cytotoxic medicines production in secure high-quality production systems, and this will require active government support at the start and appropriate regulatory frameworks. This is a policy field where incremental and collaborative innovation between health, industrial, regulatory and research actors can generate large benefits for patients and the broader industrial economy. There is an interest coalition that can be built locally to raise the local manufacturing ambition in oncology.

Notes

1. Figures for each country are from the most recent national household budget surveys, see references. Sources for exchange rates for stated dates: Bank of Tanzania historical rates, https://www.bot.go.tz/ExchangeRate/previous_rates; Central Bank of Kenya

historical exchange rates, https://www.centralbank.go.ke/rates/forex-exchange-rates/, both consulted 16/08/22.
2. https://www.aspenapi.com/api-portfolio/ last consulted 04/10/2023
3. https://aspenshare.co.za/v/rl9I0xCKbcwJig4Frgag last consulted 04/10/2023
4. https://www.aspenpharma.com/high-potency-cytotoxics/ consulted 14/07/2022.
5. https://comtrade.un.org/.
6. 6-digit classification 300,490; major product groups such as penicillin (300,410), other antibiotics (300,420), anti-malarials (300,460) are listed separately.
7. Author's personal experience.
8. Author's calculation (Chaudhuri) from DGCI&S data base, https://tradedx.cmie.com/, June 2021.
9. Calculated from the DGCI&S database (from: https://tradedx.cmie.com/, June 2022).
10. https://ec.europa.eu/commission/presscorner/detail/en/QANDA_21_521.
11. https://ec.europa.eu/commission/presscorner/detail/en/QANDA_21_521 last consulted 20/02/2023
12. https://www.gov.za/speeches/media-statement-commissioner-investigation-manufacturers-cancer-drugs-13-jun-2017-0000 consulted 15/08/2022
13. https://www.clintonhealthaccess.org/chai-and-acs-announce-agreement-to-expand-cancer-access-partnership/.
14. Details of the initiative, including prices charged, amounts actually ordered and received to date, and the incentives for firms to sustain delivery, were not found to be available at the time of writing.
15. It was also noted that radiotherapy cannot be given without permission from the national regulator: the Tanzania Atomic Energy Commission.
16. Author's personal knowledge (Ngoma).